page 62, line 2. Also, the specification has been amended to update the status of the cited related applications.

Turning now to the Office Action, the obviousness-type double patenting rejection of Claims 1, 4, 5 and 19-24 based on Serial No. 08/478,967 and of Claims 19-20 based on Claim 18 of copending patent application Serial No. 08/475,813, is acknowledged. Upon an indication that this case is otherwise allowable, Applicants will submit a Terminal Disclaimer to obviate both of these rejections.

The objection to the drawings is acknowledged. Similarly, upon the indication that this case is otherwise allowable, Applicants will submit formal figures to remove this rejection.

The objection to the trademarks "MILLI-Q" and "ALCONOX" is acknowledged. Applicants respectfully submit that no amendment of the specification is necessary because "MILLI-Q" comprises a well known water purification system. Similarly, "ALCONOX" is a well known surfactant. Therefore, the meaning of these terms would be clear to one skilled in the art. In support thereof, Applicants attach to this Reply a copy of catalog pages describing the "MILLI-Q" water purification system and the "ALCONOX" surfactant. Applicants also respectfully note that neither of these trademark materials is necessary to enable or otherwise describe the claimed invention. Therefore, withdrawal of the objection to the specification is respectfully requested.

The objection to the specification for failing to update the status of the related applications is also acknowledged. It is

believed that this objection should be moot based on the present amendment. Further, the incorrectly identified serial number has been corrected. Withdrawal of this objection is therefore respectfully requested.

The objection to the specification at page 22, line 21, has been corrected by the insertion of the corresponding Sequence identifier. Withdrawal of this objection is therefore respectfully requested.

Claims 1, 2, 4, 5 and 19-24 stand rejected for failing to be enabled by the as-filed disclosure. Essentially, the Examiner concludes that these claims are non-enabled absent assurances that the subject chimeric anti-CD20 antibody (more specifically the cell line which secretes this antibody) has been deposited in accordance with 37 C.F.R. §1.808. In particular, while the Examiner acknowledges that a transfectoma secreting this antibody has been publicly deposited, the application does not state that this cell line will be made irrevocably available. In this regard, Applicants respectfully advise that this cell line, ATCC Deposit Number 69119, was deposited on November 9, 1992, in accordance with the Budapest Treaty at the American Type Culture Collection. Moreover, this deposited cell line will be made irrevocably available upon issuance of a patent to this application or any application claiming benefit of priority to this application.

Therefore, withdrawal of the enablement rejection of Claims 1, 2, 4, 5 and 19-24 is respectfully requested.

Claims 19 and 20 stand rejected under 35 U.S.C. §103 as being unpatentable over Grossbard in view of Anderson et al. This rejection is respectfully traversed.

Grossbard discloses the use of unlabeled anti-CD20 antibody, followed by the administration of radiolabeled anti-CD20 antibody for the treatment of B-cell lymphoma. Therefore, the Examiner reasons that it would have been obvious to have produced a chimeric anti-CD20 antibody constant murine variable and human constant regions in order to derive the advantages of chimeric vis-a-vis murine antibodies (presumably reduced immunogenicity).

However, this rejection is respectfully traversed on the basis that this reference fails to teach or suggest the specific chimeric antibody of the claimed invention. Applicants respectfully note that the subject claims are directed to administration of a specific chimeric antibody having specific therapeutic properties.

Applicants respectfully note that it would not have been suggested based on Grossbard that the specific chimeric antibody of the present invention would be obtained, much less that it would possess the desirable therapeutic properties of the chimeric antibody of the present invention.

In this regard, the attention of the Examiner is respectfully referred to the substantial information, in particular at pages 46-56 of the subjection application, which relates to the beneficial therapeutic properties of the subject chimeric anti-

body when administered to non-human primates (cynomolgus monkeys) and to humans.

Moreover, Applicants also attach to this Reply a copy of a recent Press Release by IDEC Pharmaceuticals which provides further information as to the therapeutic efficacy of this chimeric antibody (referred to as IDEC-C2B8 therein) both when administered by itself and when administered in combination with chemotherapeutic agents. For example, Applicants note that of the patients who were administered this antibody there was a 100% overall response rate, with 66% having achieved a total response (absence of expression of antigen which is characteristic of B-cell lymphoma). Quite clearly, it could not have been predicted based on Grossbard that the C2B8 antibody could be obtained, much less that it would possess such therapeutic activity.

The addition of Anderson et al further does not render the claimed invention obvious. This reference is an abstract which refers to the C2B8 chimeric antibody and the murine antibody from which it was obtained. Moreover, the references discloses *in vitro* properties which indicate that this antibody may possess therapeutic potential for treatment of B-cell lymphoma.

However, notwithstanding this fact, the reference does not render the subject chimeric antibody or its therapeutic usage unpatentable. Applicants respectfully submit that this reference is deficient because it does not contain sufficient information to enable one skilled in the art to produce this specific chimeric antibody absent undue experimentation.

For example, the reference fails to disclose the amino acid sequence or a DNA sequence encoding this specific chimeric antibody. Nor does this reference refer to a publicly available source of this chimeric antibody. Essentially, the mere mention of this antibody and general *in vitro* properties is insufficient to render this specific antibody unpatentable because it does not provide an enabling disclosure.

In this regard, Applicants respectfully note that for a proper rejection the references, alone or in combination, must enable the claimed invention, absent undue experimentation. However, this burden is not satisfied herein given the highly unpredictable and essentially empirical nature of monoclonal antibody production. Applicants respectfully note that when any given antigen is used as an immunogen for antibody production, it typically gives rise to a myriad of different antibodies being produced, having different combinations of properties, e.g., epitope to which it binds, isotype, antigen affinity and avidity, serum half-life, complement function, as well as other antibody effector functions.

Given this high level of unpredictability, the mere mention of this antibody would not enable its production or its identification and isolation from a population of anti-CD20 antibodies. In further support of this argument, Applicants submit a copy of a Declaration by Darrell Anderson, Ph.D., an inventor of this application, submitted during prosecution of the corresponding European application.

In this Declaration, Dr. Anderson asserts that in his expert opinion this abstract does not contain information which would be sufficient to allow one skilled in the art to make or otherwise obtain this antibody. Moreover, the Declarant expressly note that this antibody or a cell line which produces this antibody had not been made publicly available prior to the filing date of this application.

Therefore, withdrawal of the §103 rejection of Claims 19 and 20 based on Grossbard taken in view of Anderson et al is respectfully requested.

Claims 1, 2, 4, 5, and 21-24 further stand rejected under 35 U.S.C. §103 as being unpatentable over Robinson et al (WO 88/04936) taken in view of Anderson et al. This rejection is also respectfully traversed.

Robinson et al is cited for its disclosure that anti-CD20 antibodies, and chimeric anti-CD20 antibodies specifically may be used as therapeutics. However, as acknowledged by the Examiner, the reference fails to teach the specific chimeric anti-CD20 antibody of the present invention. Thus, it does not teach the invention as a whole, as is required for a proper §103 rejection.

The addition of the Anderson et al abstract does not compensate for the deficiencies of Robinson et al for the reasons et forth *supra*. Essentially, while the reference mentions the C2B8 antibody, the reference does not contain sufficient information to allow one skilled in the art to make or otherwise obtain this specific chimeric anti-CD20 antibody absent undue experimenta-

tion. This is substantiated by the Declaration of Darrell Anderson, attached to this Reply. As noted above, this Declaration was submitted during prosecution of the European counterpart. Moreover, after submission of this Declaration, similar claims to those of the present invention were found to be patentable over Anderson et al. While the EP decision is not binding on the U.S. Patent Office, it provides further evidence that the Anderson et al abstract does not render the claimed invention unpatentable given its non-enabling disclosure.

Therefore, withdrawal of the §103 rejection of Claims 1, 2, 4, 5, and 21-24 based on Robinson et al taken in view of Anderson et al is respectfully requested.

Based on the foregoing, this application is believed to be in condition for allowance. A Notice to that effect is respectfully solicited.

However, if any issues remain outstanding, the Examiner is respectfully requested to contact the undersigned so that prosecution of this application may be expedited.

Respectfully submitted,

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